

CLAIMS

1        1        Method for characterizing the state of a neoplastic disease in a subject, comprising

5            (i)        determining the pattern of expression levels of at least 6, 8, 10, 15, 20, 30, or 47 marker genes, comprised in a group of marker genes consisting of SEQ ID NO:1 to 165, in a biological sample from said subject,

10           (ii)        comparing the pattern of expression levels determined in (i) with one or several reference pattern(s) of expression levels,

15           (iii)        characterizing the state of said neoplastic disease in said subject from the outcome of the comparison in step (ii).

20        2        Method for characterizing the state of a neoplastic disease in a subject, comprising

15           (i)        determining the pattern of expression levels of at least 6, 8, 10, 15, 20, 30, 47 or 67 marker genes, comprised in a group of marker genes consisting of SEQ ID NO:1 to 165 and 472 to 491, in a biological sample from said subject,

25           (ii)        comparing the pattern of expression levels determined in (i) with one or several reference pattern(s) of expression levels,

3        3        Method for detection, diagnosis, screening, monitoring, and/or prognosis of a neoplastic disease in a subject, comprising

20           (i)        determining the pattern of expression levels of at least 1, 2, 3, 5, 10, 15, 20, 30, or 47 marker genes, comprised in a group of marker genes consisting of SEQ ID NOs:1 to 17, 19 to 33, 35 to 50, 52 to 64, 66 to 85, 88 to 91, and 93 to 165 in biological samples from said subject,

25           (ii)        comparing the pattern of expression levels determined in (i) with one or several reference pattern(s) of expression levels,

30           (iii)        detecting, diagnosing, screening, monitoring, and/or prognosing said neoplastic disease in said subject from the outcome of the comparison in step (ii).

4 Method for detection, diagnosis, screening, monitoring, and/or prognosis of a neoplastic disease in a subject, comprising

(i) determining the pattern of expression levels of at least 1, 2, 3, 5, 10, 15, 20, 30, 47, or 67 marker genes, comprised in a group of marker genes consisting of SEQ ID NOs:1 to 17, 19 to 33, 35 to 50, 52 to 64, 66 to 85, 88 to 91, and 93 to 165 and 472 to 491 in biological samples from said subject,

(ii) comparing the pattern of expression levels determined in (i) with one or several reference pattern(s) of expression levels,

(iii) detecting, diagnosing, screening, monitoring, and/or prognosing said neoplastic disease in said subject from the outcome of the comparison in step (ii).

5 10 Method of any of claims 1 to 4, wherein said method comprises multiple determinations of a pattern of expression levels, at different points in time, thereby allowing to monitor the development of said neoplastic disease in said subject.

6 15 Method of claim 1 or 2, wherein said method comprises an estimation of the likelihood of success of a given mode of treatment for said neoplastic disease in said subject.

7 Method of claim 1 or 2, wherein said method comprises an assessment of whether or not the subject is expected to respond to a given mode of treatment for said neoplastic disease.

8 Method of claim 6 or 7, wherein a predictive algorithm is used.

9 Method of claim 8, wherein the predictive algorithm is a Support Vector Machine.

20 10 Method of any of claims 6 to 9, wherein said given mode of treatment

(i) acts on cell proliferation, and/or

(ii) acts on cell survival, and/or

(iii) acts on cell motility, and/or

(iv) is an anthracycline based mode of treatment, and/or

25 (v) comprises administration of epirubicin and/or cyclophosphamide.

11 Method of treatment for a subject afflicted with a neoplastic disease, comprising

- (i) identifying the most promising mode of treatment with the method of claim 6 or 7,
- (ii) treating said neoplastic disease in said patient by the mode of treatment identified in step (i).

12 Method of screening for subjects afflicted with a neoplastic disease, wherein a method of any of claims 1 to 4 is applied to a plurality of subjects.

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13 Method of screening for substances and/or therapy modalities having curative effect on a neoplastic disease comprising

- (i) obtaining a biological sample from a subject afflicted with said neoplastic disease,
- (ii) assessing, from said biological sample, using the method of claim 6 or 7, whether said subject is expected to respond to a given mode of treatment for said neoplastic disease,
- 10 (iii) if said subject is expected to respond to said given mode of treatment, incubating said biological sample with said substance under said therapy modalities,
- (iv) observing changes in said biological sample triggered by said test substance under said therapy modalities,
- 15 (v) selecting or rejecting said test substance and/or said therapy modalities, based on the observation of changes in said biological sample under (iv).

14 Method of screening for compounds having curative effect on a neoplastic disease comprising

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- (i) incubating biological samples or extracts of these with a test substance,
- (ii) determining the pattern of expression levels of at least 1, 2, 3, 5, 10, 15, 20, 30, or 47 marker genes, comprised in a group of marker genes consisting of SEQ ID NO:1 to 17, 19 to 33, 35 to 50, 52 to 64, 66 to 85, 88 to 91, and 93 to 165 in said biological sample,

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- (iii) comparing the pattern of expression levels determined in (ii) with one or several reference pattern(s),
- (iv) selecting or rejecting said test substance, based on the comparison performed under (iii).

15 Method of screening for compounds having curative effect on a neoplastic disease comprising

- (i) incubating biological samples or extracts of these with a test substance,
- 5 (ii) determining the pattern of expression levels of at least 1, 2, 3, 5, 10, 15, 20, 30, 47, or 67 marker genes, comprised in a group of marker genes consisting of SEQ ID NO:1 to 17, 19 to 33, 35 to 50, 52 to 64, 66 to 85, 88 to 91, and 93 to 165 and 472 to 491 in said biological sample,
- (iii) comparing the pattern of expression levels determined in (ii) with one or several reference pattern(s),
- 10 (iv) selecting or rejecting said test substance, based on the comparison performed under (iii).

16 Method of any of claims 1 to 15 wherein said marker genes are comprised in a group of marker genes listed in Table 2.

17 Method of any of claims 1 to 16, wherein the expression level is determined

- 15 (i) with a hybridization based method, or
- (ii) with a hybridization based method utilizing arrayed probes, or
- (iii) with a hybridization based method utilizing individually labeled probes, or
- (iv) by real time real time PCR, or
- (v) by assessing the expression of polypeptides, proteins or derivatives thereof, or
- 20 (vi) by assessing the amount of polypeptides, proteins or derivatives thereof.

18 Method of any of claims 1 to 17, wherein the neoplastic disease is breast cancer.

19 A kit comprising at least 6, 8, 10, 15, 20, 30, or 47 primer pairs and probes suitable for marker genes comprised in a group of marker genes consisting of

- 25 (i) SEQ ID NO:1 to SEQ ID NO:165, or
- (iii) the marker genes listed in Table 2.

20 A kit comprising at least 6, 8, 10, 15, 20, 30, 47, or 67 primer pairs and probes suitable for marker genes comprised in a group of marker genes consisting of

- (i) SEQ ID NO:1 to SEQ ID NO:165, and/or
- (ii) SEQ ID NO:472 to SEQ ID NO:491, or
- 5 (iii) the marker genes listed in Table 2.

21 A kit comprising at least 6, 8, 10, 15, 20, 30, or 47 individually labeled probes, each having a sequence comprised in a group of sequences consisting of SEQ ID NO:331 to SEQ ID NO:471.

22 A kit comprising at least 6, 8, 10, 15, 20, 30, 47 or 67 individually labeled probes, each 10 having a sequence comprised in a group of sequences consisting of SEQ ID NO:331 to SEQ ID NO:471 and SEQ ID NO:512 to 571.

23 A kit comprising at least 6, 8, 10, 15, 20, 30, or 47 arrayed probes, each having a sequence comprised in a group of sequences consisting of SEQ ID NO:331 to SEQ ID NO:471.

24 A kit comprising at least 6, 8, 10, 15, 20, 30, 47 or 67 arrayed probes, each having a 15 sequence comprised in a group of sequences consisting of SEQ ID NO:331 to SEQ ID NO:471 and SEQ ID NO:512 to 571.